

AMENDMENTS TO THE SPECIFICATION

Please amend paragraphs [0225], [0230], [0243]-[0253], [0259]-[0262], [0266], and [0267] as follows. (All paragraph numbers used in this paper refer to the specification as published, no. US 2005/0036147. However, please note that the previous specification amendment—submitted with the response to the May 3, 2006 office action—has already been incorporated into these paragraphs, where appropriate.)

[0225] In certain other embodiments in which the sample comprises blood, the absorption baseline is defined to be the magnitude of the absorption spectrum at an isosbestic wavelength at which water and a whole blood protein have approximately equal absorptions. In such embodiments, the absorption spectrum is shifted to a selected value at the isosbestic wavelength by adding or subtracting a constant offset value across the entire wavelength spectral data set. In addition, the shifting of the absorption spectrum can be performed nonlinearly (e.g., shifting the portions of the absorption spectrum in different wavelength ranges by different amounts). Shifting the absorption spectrum such that the absorption is set to some value (e.g., 0) at a protein-water isosbestic point preferably helps remove the dependence on ~~hematocrit~~hemoglobin level of the overall spectrum position relative to zero. For samples comprising plasma containing whole blood protein, similar techniques can be applied.

[0230] The goal of the spectroscopic analysis is to derive the ratio of the analyte volume (for example, glucose volume) to the total blood volume using essentially artifact-free spectra. The blood samples are primarily a mixture of three components: plasma, hematocrit soup and glucose as illustrated in FIG. 22. As illustrated in FIG. 22, "hematocrit soup" comprises the combination or mixture of the components of blood other than the plasma and glucose components.

[0243] In certain embodiments, the method uses the optical density (OD) for a parallel cuvette, parallel illumination and “delta-function” filter, which can be expressed as:

$$OD_i = (c_w \alpha_{wi} + c_p \alpha_{pi} + c_g \alpha_{gi}) \cdot d \quad (1)$$

- [0244] where:
 [0245] d = cuvette path length;
 [0246] c_w = water volume concentration;
 [0247] c_h = hematocrit soup volume concentration;
 [0248] c_g = glucose volume concentration;
 [0249] α_{wi} = water absorption at wavelength ' i ';
 [0250] α_{hi} = hematocrit soup absorption at wavelength ' i '; and
 [0251] α_{gi} = glucose absorption at wavelength ' i '.

[0252] The absorption of the various components (e.g., α_{wi} , α_{hi} , α_{gi}) at various wavelengths is a property of the components themselves, and can be known or provided to the system for use in the calculation of the analyte concentrations. In various embodiments described below, the blood sample is modeled as a three-component mixture of water, hematocrit soup, and glucose (i.e., $c_w + c_h + c_g = 1$). Other embodiments can model the blood sample with more components, fewer components, or different components.

[0253] In certain embodiments, the method uses three two-wavelength sets. The first set is in the wavelength region where water absorption dominates. The second set is in a region where water and hematocrit soup absorptions dominate, and the third set in a region where absorptions from all three components dominate. In certain embodiments, the calculations are based on OD differences of each wavelength pair to reduce or minimize offsets and baseline drift errors. Absorption values for the three components at each of the six wavelengths are shown in Table 1:

Wavelength	α_{wi}	α_{hi}	α_{gi}
1	α_{w1}	0	0
2	α_{w2}	0	0
3	α_{w3}	α_{h3}	0
4	α_{w4}	α_{h4}	0
5	α_{w5}	α_{h5}	α_{g5}
6	α_{w6}	α_{h6}	α_{g6}

[0259] In certain embodiments, the "water free" absorptions at wavelengths 3 and 4 are used to calculate the quantity B which is proportional to the product of the hematocrit soup

concentration and path length. The quantity B can be termed the “hematocrit soup scaling factor,” and can be expressed by the following relation:

$$B = \frac{OD'_4 - OD'_3}{\alpha_{h4} - \alpha_{h3}} = c_h d. \quad (14)$$

[0260] In certain embodiments in which the values of hematocrit soup absorption at the two wavelengths is known or provided to the system, this ratio of the difference of two “water free” OD values with the difference of two reference absorption values for hematocrit soup at the same wavelengths yields a hematocrit soup scaling factor B indicative of the amount of hematocrit soup in the sample.

[0261] By using B and the hematocrit soup absorptions at each wavelength, the “glucose only” OD is calculated in certain embodiments to be expressed by the following relation:

$$OD''_i = OD'_i - B\alpha_{hi}. \quad (15)$$

[0262] In this way, the “glucose only” OD value equals the measured OD value minus the scaled reference absorption values for water and for hematocrit soup.

[0266] The desired ratio of glucose volume to total blood volume can then be expressed (using the relation $c_w + c_h + c_g = 1$) by the following relation:

$$[[C_g]] \underline{c_g} = \frac{c_g * d}{(c_w + c_h + c_g) * d} = \frac{C}{A + B + C}. \quad (19)$$

[0267] By taking the ratio of the glucose scaling factor to the sum of the water scaling factor, the hematocrit soup scaling factor, and the glucose scaling factor, the resulting concentration ratio c_g is substantially independent of the path length of the sample. Thus, certain embodiments described herein provide a method of determining the glucose content of a blood sample independent of the path length of the blood sample.